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Hydrocolpos in the Newborn Period

SALVATORE BATTIATA, M.D.*

Hydrocolpos is a rare disorder which is frequently neglected in the differential diagnosis of a lower abdominal mass in the newborn female infant.

According to Kereszturi,[1] Godefrey, in 1856, and Breisky, in 1879, probably described the first cases of hydrocolpos in the newborn period. Bunzel, in 1900, reported a case of a tumor of the vulva which ruptured spontaneously on the fifth day of life, yielding a milky white fluid. Since then, sporadic cases of hydrocolpos in the newborn have appeared in the medical literature.

The first review, as stated by Morris,[2] was published in 1904 by Commandeur, who found nine cases and reported one. Mahoney and Chamberlain,[3] in 1940, presented the first detailed description in the American literature and introduced 3 new cases.

In 1938 Dobszay,[4] with the aid of synthetic estrogenic compounds, provided physicians with a physiologic explanation for one of the factors in the causation of hydrocolpos. This same work substantiated the hormonal theories of Halban (1904) regarding the etiology of physiologic neonatal mastitis and physiologic neonatal vaginal bleeding.

Although hydrocolpos in the newborn period is rare, hematocolpos in pubescent girls is not unusual. Tompkins,[5] in 1939, described 118 cases. More unusual, however, is the development of symptoms from an imperforate hymen before menarche. This was described by Bowen,[6] in 1941, and led to the introduction of the terms "mucocolpos" and "mucometria." Therefore, the development of symptoms due to an accumulation of fluid behind an obstruction in the female generative tract may be said to characteristically occur at two different age levels: in the newborn, when the secretions consist of hormonally stimulated cervical and endocervical glands (hydrocolpos), and at puberty, when the secretions usually consist of the first and second menstrual flow (hematocolpos).

Two factors must be considered in the etiology of this disorder in the newborn period: 1) obstruction or gynatresia, and 2) factors which lead to the accumulation of fluid proximal to the obstruction. The obstruction, as it occurs in newborn and pubescent girls, was formerly felt to be, in all cases, an imperforate hymen. In a detailed study, including postmortem examinations, Mahoney and Chamberlain[3] concluded that atresia of the vagina was the most common cause of obstruction in the newborn infant

* Formerly Assistant Chief Resident, Children's Hospital.

and imperforate hymen the most common cause in adolescent girls at menarche.

An imperforate hymen, present at birth, will produce no symptoms if there is no accumulation of fluid behind it. With the accumulation of menstrual flow at menarche, symptoms are produced. Therefore, of all infants with an obstruction, only a small number will develop symptoms in the newborn period. The crucial question in hydrocolpos is why some infants develop an abundance of secretions and others little or none. The answer to this lies partially in the sensitivity of the glands in the infant's generative tract, and the level of circulating maternal estrogens in the infant.

In hydrocolpos there is an accumulation of nonbloody fluid in the vaginal canal which is obstructed by an intact hymen, vaginal atresia, or a retrohymenal membrane. If the uterus is also involved, the disorder is referred to as "hydrometrocolpos." If the fluid is bloody, the term "hematometrocolpos" is used. If the obstruction is at the cervical os and the vagina is not involved, the term used is "hydrometros" or "hematometros." The importance of early recognition of these disorders lies in the prevention of

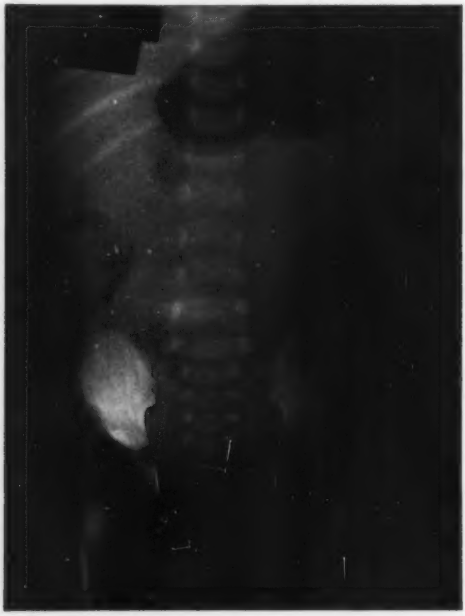

FIG. 1. Case 1. Flat plate of the abdomen demonstrating a midline lower abdominal mass displacing the bowel laterally.

irreversible damage to the generative organs and to the adjacent renal structures. Keeping the disorder in mind will insure both the correct diagnosis and the prevention of unnecessary surgery.

The two cases presented will demonstrate the two clinical types of obstruction: imperforate hymen and vaginal atresia.

CASE REPORTS

Case 1.

A 16 day old white female infant was brought to Children's Hospital because of a mass protruding between the labia. The mass, first noted on the first day of life by the mother, was bluish white and fluctuant, and was getting progressively larger and protruding.

The patient had not voided in 24 hours. Bowel movements had been normal up until one day prior to admission, when loose stools were noted. There had been vomiting after feedings for the two days prior to hospitalization.

Admission physical examination disclosed a large, firm lower abdominal mass extending up to the umbilicus. The external genitalia were normal except for the bluish white mass protruding between the labia. On rectal examination a large mass anterior to the rectum and arising from the pelvis was palpable.

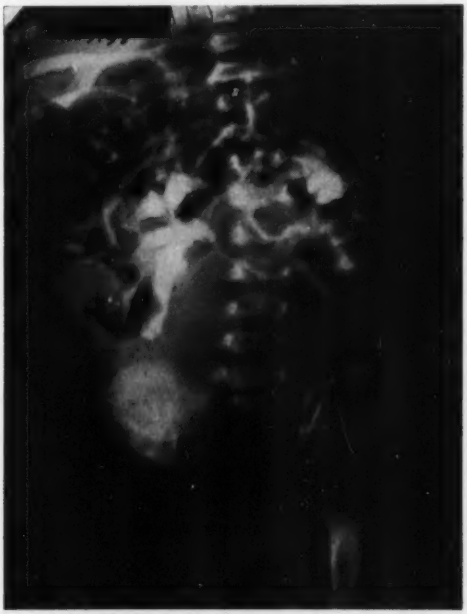

FIG. 2. Case 1. Excretory urogram showing bilateral hydroureter and hydronephrosis with lateral displacement of the dilated ureters. Note absence of dye in bladder.

Roentgenograms of the abdomen confirmed the presence of the mass (fig. 1). Excretory pyelography revealed good renal function, but there was evidence of bilateral hydroureter and hydronephrosis (fig. 2). The ureters were displaced laterally. At the end of 120 minutes there was some dye in the bladder which appeared to be displaced to the left. These changes were interpreted to suggest hydrocolpos.

Laboratory studies obtained on admission were within normal limits except for a slight metabolic acidosis and an elevated blood urea nitrogen.

Without anesthesia, needle aspiration of the mass was productive of a yellowish fluid. A clamp was then introduced to enlarge the opening, and 75 to 100 cc. of yellowish fluid was ejected a distance of some 10 feet. On culture this material was sterile.

Following this operative procedure the abdomen became soft. A Foley catheter was inserted to maintain the hymenal opening. Three days later, the patient was urinating well and the drain was removed. The cervix was visualized and fluid was escaping from the external os. The patient was discharged to be followed in clinic.

Case 2.

A 3½ month old Negro girl was in good health until three weeks prior to admission. At that time she had loose bowel movements and evidence of a pharyngitis. She was seen by a private physician who prescribed antibiotics. The pharyngitis apparently responded to treatment, but the infant remained restless and irritable. When seen again by the physician, enemas were prescribed because of a "firm hard abdomen"

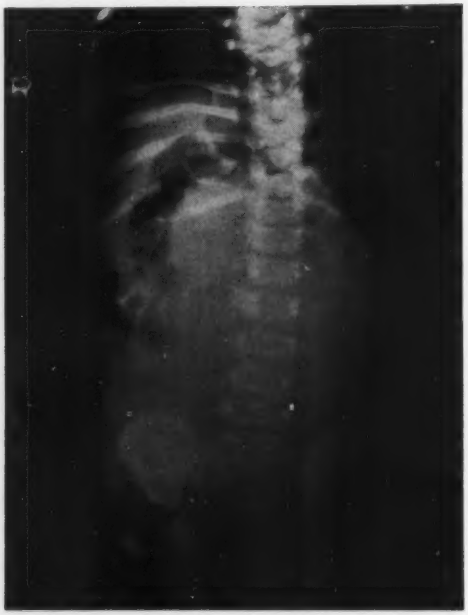

FIG. 3. Case 2. Flat plate of the abdomen showing a large abdominal mass which represents hydrometrocolpos and urinary bladder.

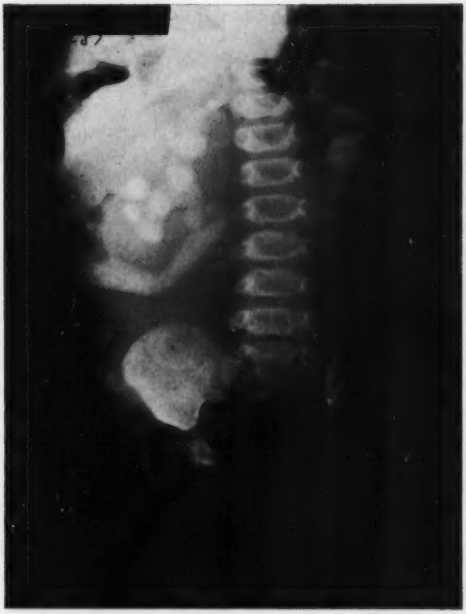

FIG. 4. Case 2. Excretory urogram showing a large abdominal mass, bilateral hydroureter and hydronephrosis. Note absence of dye in bladder and lateral displacement of the dilated ureters.

which was attributed to gas. The loose bowel movements persisted and two weeks before hospitalization, a decrease in urinary output was noted. One day prior to admission a protuberance on the right side of her abdomen and swelling of both legs was noted.

Admission physical examination at Children's Hospital revealed a distended abdomen showing a superficial venous pattern. There did not appear to be any swelling of the extremities. Catheterization did not result in diminution of the abdominal mass. There was considerable pyuria, and *Bacillus proteus* and *Aerobacter aerogenes* were cultured from the urine. The blood urea nitrogen was slightly elevated and there was evidence of anemia and leukocytosis.

With a presumptive diagnosis of Wilms's tumor, x-ray examination of the abdomen was immediately performed and demonstrated a large central opacity filling the lower abdomen (fig. 3). Intravenous pyelogram revealed bilateral ureterectasis and pyelectasis (fig. 4). Cystogram demonstrated enlargement of the bladder with lateral displacement by an abdominal mass, now thought to be a mesenteric or ovarian cyst.

A surgical consultant felt the mass was retroperitoneal and not associated primarily with the urinary tract. The provisional diagnosis was a neuroblastoma, and an exploratory laparotomy was advised. At surgery, a large mass was found and a biopsy taken. Incision resulted in prompt drainage of a sweet smelling purulent material, sterile on culture. A drain was inserted and the abdomen closed. Pathological

examination of the "cyst" wall showed foci of necrosis, in addition to "smooth muscle, fat and fibrous tissue, and thick walled arteries."

The postoperative course was uneventful and a repeat pyelogram demonstrated a decrease in the hydroureter and hydronephrosis. She was discharged one month after admission.

After being at home for one month, the patient was readmitted with a four day history of fever, anorexia, and oliguria. Pyelogram again showed ureterectasis and pyelectasis. The ureters were still displaced laterally. Cystogram showed the bladder to be still larger than normal. Urine culture grew out *Escherichia coli* and *Candida parakrusei*.

Under general anesthesia pelvic examination revealed no opening into the vaginal tract. The cervix was neither seen nor palpated. There was a thick septum extending from the posterior urethra to the posterior vaginal wall. Because of the thickness of the wall and the danger of probing blindly, a laparotomy was performed. When the peritoneal cavity was entered, the uppermost portion of the mass was identified as fundus of the uterus. The uterine cavity was entered and a viscous yellow exudate poured out. Digital probing along the course of the vagina resulted in perforation of the thick membrane, allowing drainage from the vagina. Drains were inserted into the uterus from both the vagina and the abdominal incision. Micrococci were cultured from the uterus and a diagnosis of pyometrocolpos was established. Again the postoperative course was uneventful.

Three months later, the patient was readmitted and radiographic evidence of the pelvic mass persisted. Two years after the third admission, intravenous pyelogram showed slight but persisting hydroureter and hydronephrosis. The bladder was still dilated and displaced upward.

DISCUSSION

It has been known for some time that the vagina, like the uterus, can be stretched to enormous proportions, producing a cystic mass.[1] With dilatation of the vagina, the fornices are obliterated, so that on gross examination the junction of the uterus and vagina cannot be distinguished. Besides an enlarging abdominal mass, the initial symptom of hydrocolpos may be edema and/or cyanosis of the lower extremities. This is usually due to compression of the pelvic vessels and lymphatics.[2] The main abdominal swelling is the bladder. After catheterization a much smaller second swelling, the hydrocolpos, is noted in the lower abdomen.

When hydrocolpos is caused by an imperforate hymen, there is usually a bulging membrane, but this membrane may be apparent only with crying or bearing down (fig. 5). With vaginal atresia (fig. 6), the usual presenting symptom will be a lower, usually midline, abdominal mass. On examination, the external genitalia may be normal. With progressive enlargement of the mass the bladder is displaced upward, stretching the urethra and bladder neck and resulting in urinary stasis, which, if it persists, will result in infection and renal damage.

Signs of intestinal obstruction may be due to compression of the sigmoid colon or rectum; if the compression of the bowel is partial, allowing only the passage of water, the presenting symptom may be diarrhea. As the

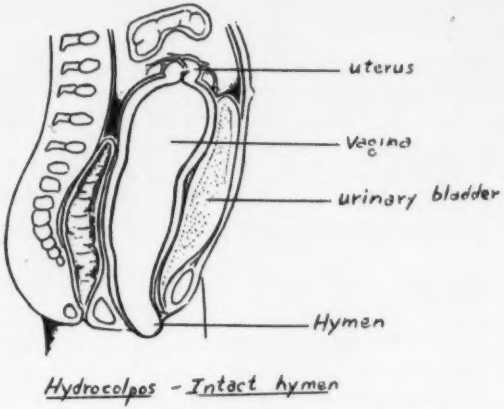

FIGURE 5

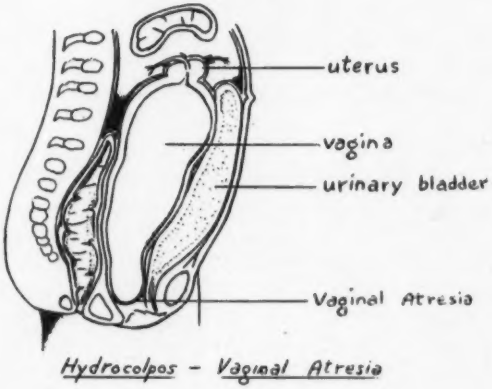

FIGURE 6

cystic mass rises above the umbilicus, displacement of the stomach may lead to progressive vomiting and electrolyte imbalance. The mass may cause respiratory embarrassment by interfering with diaphragmatic motion.

Embryology

The embryological defect which causes the atresia and forms the obstruction in hydrocolpos can occur at any point. After migration and fusion of the various *anlagen*, they exist as solid cords which acquire lumens by

dissolution of the cells in the center of the cord in a manner analogous to formation of the lumen of the intestine. Thus, the basis for the atresia is failure of complete dissolution of the central cells of the genital cords.

The male vertebrate embryo does not elaborate any ducts intended for its own sexual structures. The mesonephric, or Wolffian, duct and some of its tubules are converted into genital canals. Both male and female embryos, however, develop a pair of Müllerian, paramesonephric or female ducts. These appear in the 10 mm. embryo as a thickening along each urogenital ridge which then grows caudad. Near the cloaca the ducts fuse to form a genital cord.

With the development of the adrenal glands and the kidneys the urogenital ridges are forced laterad. This displacement of the Müllerian ducts results in two bends along its course, which roughly establishes three regions different in future potentialities. The cranial portions form the uterine, or Fallopian, tubes; the middle portions form the uterine fundus and corpus, and the caudal portions, the uterine cervix and upper vagina. The vagina is formed in its upper two thirds by a combination of Wolffian and Müllerian ducts, while the lower two thirds comes from the urogenital sinus which is of entodermal origin.

The hymen itself arises at the site of Müller's tubercle as a dorsal semilunar fold between the future vagina and the urogenital sinus.

Physiology

Dobszay,[4] in 1938, was able to reproduce in older infants with the administration of estrogens the same clinical, histological, chemical, and bacteriologic conditions present in the first few days of life.

Normally at birth there is a certain amount of viscid mucoid discharge from the vagina. This represents the changes taking place in the vaginal epithelium in response to maternal estrogens. Edema of the vulva and clitoris are also responses to maternal estrogens. The main change produced by estrogenic hormones is vaginal epithelial destruction with release of glycogen and increasing amounts of glycolytic ferments. The change of the chemical environment of the vagina to a strongly acid pH is due to the action of these tissue ferments.

According to Antell,[7] Philip and Neumann, and Peter showed that great quantities of estrogenic hormones can be found in cord blood or in the blood and urine of the newborn of both sexes. It is known that the estrogenic levels vary from woman to woman, for variable amounts of estrin are obtained from the urine of pregnant women. To substantiate the fact that the genital tract is under the influence of estrogens during the neonatal period, Mahoney and Chamberlain[3] gave histologic evidence that the appearance of the cells in the newborn genital tract resemble those of the adult female.

Even the bacterial flora are dependent on maternal hormones. The vagina is free of bacteria until a few hours after birth. At this time a mixed flora predominates, Gram-positive and negative cocci, Gram-negative rods and short-chained Streptococci. On the second day a luxuriant mixed culture is present. Then, as the maternal estrogenic effect causes a drop in vaginal pH, Doederlein's bacilli enter and proliferate until four to six days after birth when they predominate. However, this phase is short lived; two or three days later, the flora again changes until the fourteenth day, when the Doederlein bacilli have disappeared, and the mixed flora of childhood are once again present. This is associated with the drop in circulating maternal estrogens in the newborn and a rise of the vaginal pH to neutral.

As can be expected, with an imperforate hymen the acidification and discharge will occur, but will not be evident externally. The fluid contained in the vagina and uterus in hydrocolpos is simply an accumulation of the secretion of the cervical, endocervical, or, if the obstruction is at the hymen, vaginal glands. If the obstruction is in the cervical canal or upper vagina, the fluid will represent the activity of the cervical and endocervical glands only. In high vaginal atresia, the vagina will go through all the changes and there will be a vaginal discharge in response to the estrogens. Therefore, the absence of the physiologic discharge in a full term newborn infant may be suggestive of an imperforate hymen.

The cervical and endocervical glands are stimulated by the estrogenic hormones which cross the placenta, and it is presumed that their secretory activity begins *in utero* and continues for several weeks after birth, by which time the maternal estrogens are metabolized. However, there is great variability in the amount of circulating maternal hormone in the infant and in the sensitivity of the infant's cervical and vaginal glands to the hormone.

Diagnosis

The diagnosis of hydrocolpos can be made easily when the obstruction is due to an imperforate hymen, for in such a case the bulging membrane will be evident. This bulging may be seen before a palpable abdominal mass is present and before symptoms of urinary or intestinal obstruction develop.

When the obstruction is due to gynatresia, it may be several millimeters above the hymenal opening. Here the diagnosis is not so apparent because a greater accumulation of fluid is required before the thicker membrane bulges between the labia, if at all. The direction of least resistance is usually cephalad, and the presenting symptom is a palpable abdominal mass. Examination of the external genitalia is usually within normal limits and

retrospectively one may recall scanty to absent vaginal discharge in the early neonatal period.

Rectal examination is of great importance, since by this examination alone one can accurately locate the mass. It will be found arising from the true pelvis and entering the abdominal cavity, usually in a midline position and anterior to the rectum.

Signs and symptoms are all related to an abdominal mass. If the mass is large enough, respiratory embarrassment may be present due to interference with respiratory movements. There may be vomiting, diarrhea, or obstipation secondary to mechanical intestinal obstruction. Edema and cyanosis of the lower extremities, if present, are due to obstruction by the mass at the pelvic brim to the venous and lymphatic flow from the lower extremities.

A prominent symptom suggesting the diagnosis in a female infant with a midline abdominal mass is anuria. Those cases with intestinal symptoms will invariably have urinary obstruction, for it is the distended urinary bladder which comprises most of the abdominal mass. After the bladder is emptied, the abdominal mass decreases in size, and a smaller mass, the hydrocolpos, is palpable. The distended vagina adjacent to the urethra causes the extrinsic obstruction and allows the bladder to distend greatly.

Once there is ureterectasis, the signs and symptoms of a urinary tract infection follow shortly. While the accumulated fluid of the hydrocolpos is sterile, there is invariably a pyelonephritis secondary to urinary stasis. Likewise, if the obstruction has been present sufficiently long to result in infection, there will usually be present significant hydroureter and hydronephrosis. Once the hydrocolpos has been corrected, this dilatation of the upper urinary tract, along with that of the bladder, disappears with time. The crucial factor is the amount of renal damage secondary to the increased hydrostatic pressure.

Diagnosis can be made by excretory urogram. The usual finding is bilateral hydroureter and hydronephrosis, and the presence of a large midline abdominal mass. There is a delay in the passage of the contrast media into the urinary bladder. The ureters are characteristically displaced laterally.

Barium studies have been used to outline the mass and demonstrate it as extrinsic to the intestinal tract.[1, 8] The introduction of radio-opaque contrast media into the vagina to outline the organ has been successfully used and described in the literature.[8-10] This procedure can be performed safely, however, only when there is a bulging membrane which has been needled and some of the milky yellow fluids removed. In cases of atresia presenting with a large abdominal mass and no bulging membrane, and where the thickness of the atretic membrane is unknown, injection of contrast media is fraught with danger.

Differential Diagnosis

Hydrocolpos in the newborn period must be differentiated from the following:

1. Primary bladder distention
2. Mesenteric cyst
3. Ovarian cyst
4. Urachal cyst
5. Urethrocele
6. Anterior meningocele
7. Embryoma, lymphoblastoma, and teratoma
8. Diverticulum of the colon
9. Intestinal duplication
10. Vaginal cysts

Since these disorders usually present as an abdominal mass, they may produce all the symptoms of hydrocolpos.

Cysts of the vagina, usually arising from aberrant remnants of the Müllerian or Wolffian ducts or the urogenital sinus, may produce symptoms similar to hydrocolpos. The epithelial lining is the same as that of the vagina and is under the influence of maternal hormones. The location of the cyst at the introitus, anterior to the hymenal orifice, and posterior to the urethra, may suggest urethrocele. If the cyst is sufficiently large the urethra may be compressed.[11]

Treatment

In instances of imperforate hymen with bulging of the hydrocolpos through the labia, aspiration of the characteristic fluid followed by simple incision is adequate. With continued drainage, serial examinations will show the vagina decreasing to normal size within a few days. It is of prime importance that, after incision, one insures that the edges of the hymen do not become adherent. This can best be achieved by insertion of a drain or Foley catheter into the vagina or removing a small portion of the hymenal membrane. Although there are no reported cases of hydrocolpos in infancy and hematocolpos at puberty due to contracture and closure of the hymen, this is well within the realm of possibility.

With vaginal atresia the treatment is more complicated. Without a bulging membrane to serve as a guide, there is danger in probing with a needle for aspiration or introduction of contrast media. Pneumoperitoneum is not without its dangers and probably does not give too much information.

Once the bladder has been emptied, perhaps the best procedure is an exploratory laparotomy, using an abdominal perineal approach.[8, 12] Under direct visualization the adnexa can be examined and the vagina entered, either through its stretched lateral wall or through the uterus, if hydro-

metrocolpos is present. With a simultaneous perineal approach one can then dissect down to the septum and incise the membrane. At surgery there may be considerable difficulty identifying structures due to the disruption of the normal anatomy; careful inspection is therefore mandatory.

The question arises as to what treatment should be instituted if on routine examination of a newborn infant what appears to be an imperforate hymen is detected in the absence of signs or symptoms to suggest hydrocolpos. The consensus is that nothing be done. Usually, these are not imperforate, but only appear so. There are usually tiny openings in the hymen which are adequate for the passage of menstrual fluid. At puberty, if there is a delay in the appearance of menstrual fluid after other signs of maturation are present or if symptoms referable to an abdominal mass develop, the possibility of an imperforate hymen should then be considered.

Another condition which may cause confusion is atresia of the entire vagina. Since there is no urgency, prudence suggests waiting until the patient is at an age when investigation can be followed by definitive plastic reconstructive surgery. This is usually at puberty or older if possible. If symptoms are present, treatment must be instituted for their relief. Definitive surgery is then instituted at the proper age.

The prognosis in hydrocolpos in infancy is usually good. When the diagnosis is made before irreversible renal damage occurs, the distended vagina soon returns to normal size, the urinary tract obstruction is relieved, and any urinary tract infection, unless caused by a highly resistant and virulent organism, responds well to the usual antibacterial treatment.

SUMMARY AND CONCLUSION

1. The diagnosis of hydrocolpos should be suggested in a newborn female infant presenting with a midline lower abdominal mass.
2. In a full term newborn female infant without any physiologic discharge from the vagina, the possibility of gynatresia should be considered.
3. Excretory urogram will reveal the abdominal mass, bilateral ureterectasis, and pyelectasis, with lateral displacement of the ureters. The diagnosis is established when the bulging membrane is needled and the characteristic fluid aspirated.

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Clinical Pathological Conference

J. William Oberman, M.D.*
Grace H. Guin, M.D.†
E. Clarence Rice, M.D.‡

PRESENTATION OF CASE

This 5 month old Negro male infant was admitted October 1 to Children's Hospital for the first time, with a chief complaint of fever of two weeks' duration. The child was apparently in excellent health until one night, about two weeks prior to admission, when the mother noticed he had fever. This was not associated with chills, but was accompanied by drenching sweats. The actual temperature was not recorded, nor did the child appear ill until about one week prior to admission, when he began to show signs of anorexia and started to become irritable. He was taken to his local physician who, on examination, found an enlarged liver and spleen. The infant was then admitted to this hospital.

On examination, this 5 month old child did not appear ill, but had a temperature of 105° F. Heart and lungs were normal. Abnormal findings were limited to his abdomen, where the liver was palpated approximately 8 cm. below the costal margin. An additional mass in the left upper quadrant extending down to the iliac crest and over to the midline was also palpated; there was a question at this time as to whether this was spleen or an abdominal mass. An intravenous urogram revealed the right kidney to be normal. On the left side, the pelvis and calyces were visualized fairly well in the four and ten minute films and seemed to be normal. The stomach appeared to be displaced far anterior and medially; this was confirmed by a barium swallow. It was the impression of the radiologist that a retroperitoneal mass was present on the left side; this was thought to be possibly a neuroblastoma, although a Wilms' tumor could not be ruled out. There was no x-ray evidence of pathology in the chest.

Initial laboratory procedures included a blood count which showed a hemoglobin of 6.2 Gm. per 100 ml. with a hematocrit of 26 per cent; the leukocyte count was 2,400 per cu. mm. with a differential count including 38 segmented neutrophils, 22 band forms, 27 lymphocytes, 4 atypical lymphocytes, and 9 monocytes. Platelets appeared to be reduced, and 10 erythroblasts per 100 red cells were seen. After blood transfusion, hemoglobin was 9.9 Gm. per 100 ml. Following several consultations, it was felt

* Associate Staff, Children's Hospital.

† Attending Staff, Director of Laboratories, Children's Hospital; Assistant Clinical Professor of Pediatrics, Georgetown University School of Medicine.

‡ Senior Advisory Staff, Department of Laboratories, Children's Hospital.

that the probable diagnosis was a retroperitoneal tumor. The child was operated on October 4.

Additional laboratory studies: Urinalyses on October 2 and 3 were within normal limits. A VDRL was negative. Daily complete blood count from the time of operation showed the hemoglobin to be rather constant at 11 Gm. The leukocytes steadily increased from 4,100 on October 3 to 7,000 on October 10. Platelet counts between October 5 and 11 ranged from 5,000 to 20,000. A reticulocyte count on October 6 was 8.2 per cent; sickle-cell preparation was negative. The infant received approximately 450 cc. of blood pre- and postoperatively. Approximately 300 cc. of this was packed cells and 100 cc. fresh blood. Bone marrow smear done preoperatively on October 2 showed evidence of active hematopoiesis. No tumor cells were seen.

Discussion

Dr. Oberman:

Briefly, this 5 month old infant probably had a fever of about two weeks duration; the fever appears to have been a sizable one since a body temperature of 105° F. was mentioned on admission, and it was at least high enough before admission to cause drenching sweats. The private physician found what he thought to be an enlarged liver and spleen, and the infant was admitted to the hospital with a diagnosis of hepatosplenomegaly.

When admitted to the hospital he had a high fever, a liver which was quite enlarged, extending 8 cm. below the costal margin, and a mass in the left upper quadrant which was also quite large, extending down to the iliac crest and over to the midline. There was some question, and I think rightly so, whether this was indeed a spleen or whether it was not. In an attempt to find out if it was, an intravenous urogram and a barium meal were done. The right kidney was normal and the left seemed to be, even though it was much less satisfactorily visualized. Barium meal showed the stomach to be displaced far anteriorly and medially; this was interpreted to mean that the mass was retroperitoneal in location.

In examining the peripheral blood count we see that this infant had what amounted to pancytopenia; he certainly had an anemia and leukopenia, and before operation, the comment was made that the platelets appeared to be reduced. However, the 10 erythroblasts per 100 red cells would indicate to me that the bone marrow was responding and perhaps overresponding. There certainly did not seem to be anything depressing the bone marrow.

At this point, I would like to ask if notation was made of any lymphadenopathy.

Dr. Guin:

There is no mention of it on the chart.

Dr. Oberman:

The probable preoperative diagnosis was a retroperitoneal tumor, and the infant was operated on, probably because those managing the case were worried about a Wilms' tumor or neuroblastoma.

As previously mentioned, a bone marrow done preoperatively showed active hematopoiesis. I wonder how vigorous a search was made at that time for the presence of organisms, and I wonder if the marrow was cultured; I would like to have had information on both. It is noted, however, that there were no tumor cells in the bone marrow. This is nice to know provided we could be assured the marrow aspiration was not made through an area where there were no tumor cells whereas they were actually present in other areas. A negative bone marrow under these circumstances does not help us much although it is a piece of adjunct information.

Urinalysis and a serologic test for syphilis were normal. After operation the anemia seemed to be corrected somewhat, but how much of this was due to transfusions we do not know, of course. The white blood cell count did rise; the reticulocyte count was 8.2 per cent, indicating again that the bone marrow was responding quite well and was capable of doing so; and at long last, after the operation, a sickle-cell preparation was obtained. I would like to have had this before operation; I would have been very embarrassed if it had been positive.

Here, then, we have a child with fever, an enlarged liver, a mass in the left upper quadrant, and pancytopenia. What does this mean to me? I think that I would prefer to think of this left upper quadrant mass as indeed a spleen, a very large spleen to be sure, and a spleen which is a bit difficult to explain because of the way the stomach is shifted. I do think that a sufficiently large spleen could explain these x-ray findings. At least I am going on this basis for the time being.

This brings us to a whole wealth of diagnoses: the causes of hepatosplenomegaly and fever in a young infant. The unusual blood findings, the pancytopenia, could be explained on the basis of a hypersplenism due to a huge spleen which is hypersequestrating or elaborating humoral substances, whichever theory you care to believe.

What are causes for hepatosplenomegaly and fever in this age period? The first group of causes we must think of, of course, are infections. Practically any infection with septicemia will produce hepatosplenomegaly in this age period. Let us return to the white blood cell differential in this infant; it is very interesting. There are 38 segmented neutrophils and 22 band forms. We do not usually get as excited about band forms in children as we do in adults, but 22 per cent band forms is a much larger number than we usually see, and I do not think we can ignore this finding. Is this an infectious process?

Before I base a diagnosis on infection I will say I am a little worried about

the size of this mass. If this is spleen, it certainly is a big one, and if this is liver, it is a big one, too. Nevertheless, any septicemic-like process can result in hepatosplenomegaly, particularly a chronic septicemic-like process, whether bacterial or otherwise. I recall at least one child with chronic salmonellosis at this hospital who presented the physical findings of hepatosplenomegaly; this was misdiagnosed and treated for quite some time as miliary tuberculosis until Salmonella organisms grew from one of the blood cultures.

This brings us to tuberculosis, and what about tuberculosis? Certainly we have no record of any skin test for tuberculosis, and whether or not such a test was positive would not discourage us from the diagnosis. Could this be tuberculosis? I do not see why not. We would like to have seen miliary pulmonary lesions in the x-rays, since, of course, this would have been a miliary type of tuberculosis involving many organs of the body. Particularly the spleen and liver in miliary tuberculosis are usually prominently involved. It is difficult to interpret chest x-ray findings in this age group, but the lung parenchyma seems only to be a little murky. The absence of miliary lesions does not negate the diagnosis since it takes time for these lesions to appear on x-ray. Tuberculosis accompanied by hypersplenism is a definite possibility here, I believe.

Ten years ago when I was a senior medical student, I was presented with a protocol, which, if I could find it, would present a case almost exactly like this one. The original infant was one with generalized histoplasmosis. Histoplasmosis at that time usually was recognized only in its generalized form. We were just beginning to learn about the more benign forms that histoplasmosis can take. As we have learned, the entire disease spectrum of histoplasmosis is far more common than we once thought, and the severe form such as this might represent is a very uncommon disease. However, this was the way we thought that histoplasmosis always presented itself a few years ago. We still do not know much about histoplasmosis; we do know that a fungus is the etiological agent but we do not know how it is transmitted except that there is some evidence that soil fertilized with the droppings of chickens is incriminated in its transmission; it has also been cultured from hollow trees. Histoplasmosis is certainly a cause of fever and hepatosplenomegaly. Again we would have appreciated seeing lesions in the chest x-rays but would not be deterred from a diagnosis by not seeing them.

Infectious mononucleosis does occur in childhood, and such a diagnosis should be thought of in any case of unexplained hepatosplenomegaly, although I have never seen it in an infant so young; however, we really have no additional information from either clinical observations or laboratory findings to substantiate such a diagnosis.

Hematopoietic disorders are frequent causes of hepatosplenomegaly in

infancy. We certainly do see sickle-cell anemia in this age group; in fact, in my personal experience, a 5 month old Negro infant with hepatosplenomegaly and anemia has sickle-cell anemia until proven otherwise. A superimposed hypersplenism may occur as a complication of any chronic hemolytic anemia and sometimes gets to be a problem. Frequently in both sickle-cell anemia and thalassemia major, as the disease progresses, the interval between transfusions may be noted to become less and less. Secondary hypersplenism, although a difficult diagnosis to substantiate, might be considered a prominent cause; in any event, in selected patients with chronic hemolytic anemia, such a diagnosis is an indication for splenectomy in order to reduce the need for transfusions. The hepatomegaly in sickle-cell anemia is not very satisfactorily explained; only a portion of the liver enlargement seems to be due to transfusion hemosiderosis. The negative sickle-cell preparation is against a diagnosis of sickle-cell anemia, although one would have liked to apply confirmatory laboratory tests. Both spleen and liver in thalassemia major may be enormously involved, and secondary hypersplenism is not uncommon; although an unlikely diagnosis in this infant, it must be considered.

Finally, among the primary disorders of the blood, leukemia must be considered, particularly leukemia in the aleukemic phase. Peripheral blood and bone marrow findings are certainly not typical, but in the clinical course of leukemia, at any given time almost any hematologic picture may be produced.

One of the lymphomas involving liver and spleen must be prominently considered in this infant. I would like to have seen some lymph node enlargement (as I would like to have seen some lymph node enlargement in practically any diagnosis we have discussed or will discuss) but am not disturbed at its absence. The neoplastic process may involve only the spleen and liver and may have not yet invaded the bone marrow, or perhaps the bone marrow specimen was obtained from an area where the cells had not yet infiltrated; this is always possible. I have gradually come to believe that in any one of these blood disorders any bone marrow picture might be presented in a given biopsy. In any event, one of the lymphomas (lymphosarcoma, reticulum cell sarcoma or Hodgkin's disease) is a real possibility.

Other potential diagnoses in this infant center around primary liver diseases with superimposed hypersplenism. A very attractive diagnosis is either congenital or posthepatitic cirrhosis. Perhaps this child had infectious hepatitis which was not diagnosed in the newborn period, or perhaps he had congenital cirrhosis, certainly a rare diagnosis, but we always remember what we see and I have seen at least one case. We have no evidence for these; however, a more detailed history and a battery of liver function tests might have been helpful.

Extrahepatic causes of hypersplenism are all fairly unusual, but a few rare retroperitoneal tumors capable of encroaching on the portal circulation, such as pancreatic neoplasms or retroperitoneal teratomas, should be considered. These are, however, unlikely.

Next we should consider a rather large group of infiltrative causes of hepatosplenomegaly, all of which are quite uncommon. These may be considered in two large groups: The lipidoses (Gaucher's, Niemann-Pick) and the reticuloendothelioses (Letterer-Siwe's, Hand-Schüller-Christian, eosinophilic granuloma). The most acute form of the reticuloendothelioses is Letterer-Siwe's disease; the subacute form, Hand-Schüller-Christian disease; and the most chronic, eosinophilic granuloma of bone. As we have learned more about these diseases we find that they blend into one another, and one form, after being present for years, may suddenly blossom into another form, and in so doing become more chronic or more acute. The basic pathology of this group is a granulomatous lesion of the cells of the reticuloendothelial system of unknown etiology. The most likely member of this group, in view of the very acute course of the disease in a young infant, is Letterer-Siwe's disease. Prominent features of this disease include lymphadenopathy, hepatosplenomegaly, thrombocytopenia and anemia, and frequently scalp lesions having the appearance of seborrheic dermatitis. This rash may also be generalized, and frequently, presumably due to the thrombocytopenia, it has a petechial character. Although we do not have anything in this case which suggests such a diagnosis, it is one to be kept in mind.

The lipidoses are also infiltrative diseases of unknown etiology in which the reticuloendothelial cells are choked with certain lipids. These would include primarily acute infantile Gaucher's disease in which the substance is kerasin, and Niemann-Pick disease in which the substance is sphingomyelin. These diseases also present with hepatosplenomegaly; we would have liked of course to find the characteristic cells in the bone marrow, since this is one of the organs involved. The only real way to differentiate these diseases and their variants is by examination of the typical cell found in the bone marrow or in biopsy from liver or spleen. In Gaucher's disease the cells are described as appearing more like tissue paper, whereas the Niemann-Pick cell is more vacuolated. Again we do not have any real evidence for either of these conditions, but they certainly must be considered in the differential diagnosis.

We have been talking a great deal about the spleen and liver; is this mass a Wilms' tumor or a neuroblastoma? I do not know whether I could really rule these out. The way that the intra-abdominal organs are shifted, whether the kidney is displaced in or out, or whether the stomach is displaced anteriorly or posteriorly, to my way of thinking does not offer much help, perhaps because I am not a radiologist. Certainly I would have no

trouble in believing that a very large spleen could also produce the roentgenographic findings. Given this age group and given this very large mass, Wilms' tumor must be considered. However, we still have not explained the enlarged liver. Wilms' tumor does not characteristically metastasize to the liver, but rather to the lungs or bones. Neuroblastoma, on the other hand, metastasizes to the liver as well as to bones. I do not know any real way we have of ruling these out from information presented in the protocol, although I do not think that either tumor is a likely diagnosis. Especially as this was thought to be a tumor, we would have to assume that there was liver metastasis, and I would have preferred to delay operation until an attempt was made to investigate other possibilities. But this is hindsight; there may have been many extenuating circumstances at the time.

This leads me to my opinion of what this infant had, and assuredly any one of the diagnoses discussed is a possibility. I think, however, I would lean very heavily on this being an infection, the most likely diagnosis being tuberculosis or histoplasmosis. As a second possibility, I would suggest a lymphoma, a condition involving primarily lymphoid tissue, because in view of the hematologic findings I still think this left upper quadrant mass is a spleen.

Dr. Guin:

In spite of the young age of the infant this is a case of overwhelming histoplasmosis. The spleen was biopsied the morning of operation and the diagnosis made on frozen section; the afternoon of operation the spleen had to be removed because of rupture. You will recall that the platelet count was depressed due to the secondary changes resulting from the infection.

The spleen in a child this age normally weighs 17 Gm.; this child's spleen weighed 153 Gm., a ten-fold increase in the size of this organ. This size spleen could certainly simulate a retroperitoneal tumor displacing the hollow organs anterior to it.

While we did not see the organisms on the smear of the bone marrow, they grew out in culture; blood smears showed Histoplasma in a few of the cells and the spleen also yielded Histoplasma on culture.

The infant was treated with amphotericin following diagnosis, but wound healing was very poor. He developed a Pseudomonas peritonitis with a paralytic ileus and intestinal obstruction which necessitated laparotomy. Wound healing again was poor. *Histoplasma capsulatum* was cultured from the wound and from the peritoneal fluid, and the infant expired a few days following operation.

At autopsy the infant was extremely jaundiced; the liver was markedly necrotic and filled with the histoplasma organisms. Grossly, the lungs showed hemorrhagic areas over the surface, and microscopically, both

areas of necrosis and numberless histoplasma organisms. The family was brought in and tested, and both parents and the seven siblings had evidence of histoplasma infection. The family lived in a rural area in Maryland not far from the District of Columbia; there was an old chicken house on the property to which the children had access, and the fungus was isolated without difficulty from soil samples taken from the vicinity. I do not know what contact this young infant had with that area, but he apparently had ample opportunity to become infected. As far as is known the remaining members of the family had not become ill, even though at the time they were tested there had been some intimation that several members of the family had episodes of slight fever or malaise for a short time; these episodes were interpreted by the family as being upper respiratory infections.

In this particular child, the infection was the most overwhelming that we have seen; Histoplasma grew out of all specimens we cultured including stool specimens. This child therefore would not have responded to treatment at his advanced state of infection.

I think that with a picture such as this, unless one had some experience with histoplasmosis and had learned to consider it as a very real possibility, he might not include it in a differential diagnosis. It must be kept in mind that tuberculosis and other infections are a very important cause of hepatosplenomegaly with fever. We have seen fever, of course, with an occult neuroblastoma which we were not able to locate or identify; fever also occurs with metastatic tumors, and it must be considered. Bone marrow depression can occur with tumors, and all of these aspects of the case which Dr. Oberman has so clearly demonstrated to you in his outline certainly do occur and must be considered. I do not recall seeing the liver so enlarged in a child with Wilms' tumor or neuroblastoma. Terminally, of course, the liver may be invaded by either one of these tumors, but it would be unusual to find at an initial diagnosis a liver this large in the presence of a Wilms' tumor or a neuroblastoma.

The bone marrow in neuroblastoma or Wilms' tumor could show depression due to the debilitated state of the patient; it could show normal myelopoiesis or metastasis. Failure to find tumor cells in bone marrow aspiration does not mean that diagnosis of tumor can be ruled out. The bone marrow occupies a very large area, and one needle of biopsy material can fail to give the proper diagnosis.

Dr. Rice:

This disease is of interest to us at Children's Hospital because it was here that the fourth case of histoplasmosis in the United States was reported.

It is interesting to go back historically to Darling's original observations in the Canal Zone when he discovered several patients who had illnesses which were thought to be kala-azar but in whom he felt that the parasite

was not morphologically the same as the organism causing kala-azar. It is also interesting in that the child who was the first one recognized at this hospital as having histoplasmosis had a history almost identical with the one we have been discussing, viz., leukopenia, increase in band forms, large liver and spleen, and fever. Examination of the bone marrow did show the organisms. However, initially we thought the diagnosis was aleukemic leukemia, and finally when the parasites were found we changed the diagnosis to kala-azar. This diagnosis was confirmed by the physician who was then head of the Division of Tropical Medicine at the Naval Medical Center. It is likely that if tissue from this child were sent to a pathologist in China he would also say that it was from a patient with kala-azar. This fourth case of the disease discovered here was actually taken to New York and exhibited at one of the medical meetings there as kala-azar in an infant, and we reported it at a meeting of the Washington Society of Pathologists. It was accepted by everyone until a physician who had been at Vanderbilt University and heard of the work being done there on histoplasmosis said, "Could this be histoplasmosis?"; that of course is what it turned out to be. Later on, Dr. Emmons of the National Institutes of Health became interested in the disease, and a great deal of the original work was done right in this area. We found that it was essentially a rural disease, and it was in the area around Leesburg where Dr. Emmons first did his soil sampling which later helped to show the role of animals and fowls in transmission of the disease.

It will not be surprising that as our population moves into dry rural areas, where there is a heavy seeding of *H. capsulatum* in the ground and in the dust of old farm buildings, that the incidence of histoplasmosis will not diminish. Most of these infections will probably be benign, and few will be likely to terminate as did this patient's illness.

The Usual Pediatric Visual Problems

MARSHALL M. PARKS, M.D.*

It is the hope of the ophthalmologist to interest the pediatrician to encompass within his sphere of preventive medicine a program designed to discover the child with poor vision and visual discomfort. Unfortunately,

* Attending Staff, Children's Hospital; Clinical Instructor in Pediatrics in Ophthalmology, Georgetown University School of Medicine; Associate Staff, Washington Hospital Center.

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the child afflicted with either or both of these disorders usually has to be discovered; he does not present himself as a patient since the way he sees is accepted as normal. The school vision screening program has performed admirably in discovering many of these patients, but it is an outstanding deficiency of current preventive medicine that such children are not found at a younger age than that afforded by the school program.

The more common pediatric visual problems can be conveniently classified into, 1) poor vision, 2) strabismus and 3) visual discomfort. Since the pediatrician is usually the first medical authority to engage ophthalmological symptoms and findings in children and infants, a brief review of the etiologies and treatments should be helpful.

Visual skill, measured in terms of proficiency in distinguishing the symbols on the Snellen Vision Chart, gradually develops as a conditioned reflex over the first 5 to 7 years of life; after 5 to 7 years of age it is extremely difficult, if not impossible, to develop this skill. If, however, treatment of the poor vision is instituted prior to 5 years of age the prognosis for improving the vision is good.

Binocular visual skill is that ability to fuse in the cortex the individual images presented to each retina. Unless this reflex has the opportunity to develop at a very young age, a bizarre abnormal method of fusing replaces the normal. A prerequisite for normal development is straight eyes. If, prior to 5 to 7 years of age, strabismus replaces straight eyes, the normal fusion pattern which developed before the onset of the strabismus can be replaced by an abnormal one. If the strabismus first appears after 7 years of age, the normal fusion persists.

Strabismus is usually obvious, and pediatricians generally refer the afflicted child for ophthalmological care while young: by 6 months of age if congenital, or as soon as it appears if over 6 months of age. The pediatrician should not be embarrassed if the case proves to be pseudostrabismus (illusion of strabismus due to epicanthi, wide flat nasal bridge, and small interpupillary distance). Such an outcome reflects an attitude of being keenly on the alert for visual problems and is to be commended.

Poor vision is not so conspicuous as strabismus and consequently has to be ferreted out. The ideal would be for the pediatrician to conduct vision screening routinely on patients as they attain 4 years of age. This is the ideal age to first test the visual acuity because, 1) this is the earliest that most children submit and respond to a subjective type examination, and 2) instituting treatment of the poor vision at this age carries an excellent prognosis.

The essential thing in the vision screening examination is to determine separately the acuity of right and left eye. The best method of doing this is to use the illiterate E Snellen Chart: the child points his finger in the direction in which the E is pointed. Charts with pictures are not encouraged

since too much depends upon whether the child has had experience with the object pictured and can recall the term that identifies it. Pictures are also of such varied shape that possibly a picture on the 20/80 line may be more easily seen than one on the 20/100 line. The test symbol should be constant in shape and graded in size; the letter E is most satisfactory for this purpose. The pediatrician should restrict his screening to determining the visual acuity; if this is found to be abnormal he should refer the child to an ophthalmologist. 20/30 vision can be accepted as normal until 7 years of age.

Poor vision can be unilateral or bilateral; it also may or may not be improvable with a lens to normal. The visual condition which is not improvable to normal is called amblyopia, which literally translated from the Greek means "dull eye." Amblyopia may be due to an organic defect such as a cloudy cornea, cataract, or malfunctioning retina or optic nerve. A much larger number of amblyopic eyes, however, have normal anatomy but are functionally dull due to disuse.

Disuse amblyopia is generally a unilateral problem. Usually a situation exists which permits normal visual acuity to develop in one eye but not the other. The two outstanding clinical conditions that cause disuse amblyopia are, 1) eyes having unequal optical qualities, 2) eyes being improperly aligned. The former is anisometropia and the latter is strabismus.

Anisometropia means unequal optical measurements between the eyes, for example, one eye is perfect while the other is farsighted. Eyes with unequal systems have a sharp image focused on only one macula while the opposite macula receives a blurred image. If the eye receiving the sharp image is used exclusively it develops good vision; conversely, the eye which receives the blurred image has no incentive to see and is amblyopic from disuse.

Strabismus, a Greek term assimilated directly into the English language, signifies improperly aligned eyes. In such a situation only one eye at a time is permitted to have the image of the object viewed projected upon its macula, rather than the usual situation where such an image is being simultaneously projected onto both maculas as it is with straight eyes. If one eye is used exclusively while the other is always deviated, visual skill will never have the opportunity to develop in the deviated eye; hence, it will be amblyopic from disuse.

Amblyopia is not a rare disorder. Approximately 3 out of every 100 infants develop disuse amblyopia in one eye unless preventive measures are started at a young age. About one half of these will be caused by strabismus, the other half by anisometropia. Although strabismus accounts for about one half of the disuse amblyopia problem, it should be stressed

that less than one half of all strabismic children develop an amblyopic eye. This is because some constantly strabismic children alternate, using the right eye one moment and the left the next. Furthermore, some children are intermittently rather than constantly strabismic. In either case each macula is stimulated sufficiently to prevent amblyopia. Still others ideally receive immediate treatment for their acquired strabismus with restoration of straight eyes before amblyopia has established a foothold.

The treatment of disuse amblyopia secondary to strabismus consists of patching the straight eye which forces the deviated eye to do the seeing. The treatment of disuse amblyopia secondary to anisometropia includes wearing lenses which compensate for the respective optical error in each eye, and occlusion of the good eye which forces reliance upon the visual information supplied by the amblyopic eye. Without occlusion the child would continue to rely upon visual information supplied by the good eye, even though glasses cause sharply focused images to be simultaneously presented to each macula. After the vision has been equalized, the glasses must be continued; otherwise, amblyopia will return.

Poor vision which is improvable by a lens is due to such optical defects as farsightedness, nearsightedness, and astigmatism. Nearsightedness (myopia), if uncomplicated by astigmatism, is more apt to cause blurred distant vision than visual discomfort. Myopia is an extensive problem affecting approximately 20 per cent of the American population. It usually begins to affect the visual acuity sometime after 7 years of age. A relatively small amount of myopia reduces the distant visual acuity considerably; for this reason a child may have 20/20 vision one year which may have dropped to 20/100 the following year. The normal eye sees clearly out to infinity whereas a 1 diopter myopic eye sees clearly only out to 40 inches (1 meter). One diopter of myopia usually reduces the visual acuity on the Snellen Chart to about 20/100, and a myopic increment of one diopter within one year is not unusual in a growing child. The hereditary aspect of myopia is very apparent. The same holds true for farsightedness and astigmatism. In fact, so significant is this that it would profit the pediatrician to inquire about the optical status of the parents' and siblings' eyes. Then, if myopia is prevalent, although the child has 20/20 vision today, the parent should be alerted to the possibility of myopia appearing sometime before full growth.

Visual discomfort is more commonly encountered in older children. This is often referred to as eyestrain because the symptoms appear during a visual pursuit that demands prolonged attention to detail. The symptoms are varied and range from congestion of the conjunctiva, tearing, smarting of eyes, foreign body sensation (sand in eyes), aching eyes, frontal headaches, blurring of near visual detail, double vision, and nausea. It may

occur in normal eyes which are taxed beyond their threshold of fatigue. Poor lighting, poor near work posture, generalized fatigue due to insufficient sleep, and a state of poor health are all factors which reduce the threshold of fatigue and hasten the onset of visual discomfort. It may also be caused by the additional visual effort required of farsighted and/or astigmatic children in obtaining sufficiently clear vision to accomplish their detailed visual task. Such would represent an optical cause for visual discomfort. A totally different cause is the compensatory effort needed to mask small misalignments of the eyes in the interest of preventing double vision. In such instances, instead of the eyes being perfectly straight they are either slightly diverged, converged, or vertically separated. Although reflexes compensate for these small misalignments, forcing the eyes to remain straight requires effort which is fatiguing. Persistence in compensating for these slight deviations after the onset of fatigue causes visual discomfort.

The treatment for either poor vision which is improvable to normal or visual discomfort usually involves the prescription of glasses. Sometimes eye exercises (orthoptics) are helpful in treating the discomfort caused by small misalignments of the eyes.

SUMMARY

The usual visual problems encountered by the pediatrician are, 1) poor vision, 2) strabismus and 3) visual discomfort.

Poor vision which is capable of being improved with a lens is caused by myopia, farsightedness, and astigmatism. Unimprovable poor vision, which is called amblyopia, is due either to an organic defect or to disuse. Disuse amblyopia must be treated prior to school age if good vision is to be obtained. Therefore, it is suggested that pediatricians institute a program of routinely determining the visual acuity of their patients at 4 years of age.

Children with strabismus should be referred to an ophthalmologist as soon as the strabismus is acquired or by age 6 months if the strabismus is congenital.

Visual discomfort is usually the result of optical errors such as farsightedness and astigmatism, or small misalignments of the eyes which are compensated.

The Editor's Column

THE RESEARCH FOUNDATION OF CHILDREN'S HOSPITAL

The Children's Hospital of the District of Columbia and its research arm, the Research Foundation of Children's Hospital, are working partners in the care and study of children. The Foundation is, in point of time, the

junior and less familiar partner; this lack of familarity should not impair an accurate assessment of the contributions made by the Foundation to both the care of individual patients and the practice of pediatrics in general. Given that their goals are jointly held, what are the benefits accruing from a relationship between a research foundation and its sponsoring children's hospital?

The effect of a research foundation upon the house staff comes high on the list, beginning with recruitment. If the purpose of a modern teaching hospital is to attract the best students from the best schools, the presence of full time teachers with active research programs is the single most powerful inducement to such students. Research personnel can provide much of the formal teaching program for the house staff, as well as provide easily available consultations and many specialized laboratory tests in several subspecialties for staff patients. Probably the most important function of a research foundation is the stimulation of the professional growth of these young physicians by providing an atmosphere of critical analysis of diagnoses and treatments; such a carryover of the self-critical attitudes of the laboratory to the bedside is of particular importance in the training of physicians. Finally, the resident physicians can get their first direct experience with research. If they are stimulated by this exposure and encouraged to continue on into the research fellowship program, we all stand to gain from the development of urgently needed research workers in pediatrics.

All of the above has obvious application to the practicing pediatrician: A better house staff means better on-the-spot care for his patients. His own professional growth is directly related to the excellence of the formal teaching program and the stimulation he receives from an academic environment. He may also share the pride of accomplishment that attends the scientific achievements of the research program.

What are the potential effects of a research foundation on the hospital itself? Reputation, attraction of the community's best physicians, and recognition in the form of grants, endowments, and public support are all dependent in large measure, on research activities of a growing hospital. Both Children's Hospital and its Research Foundation are, and should be, mutually dependent on, and synergistic to, each other's well being.

L. B. B.

Book Review

Pediatric Pathology. By DANIEL STOWENS, M. D. 676 pages, 374 illustrations. Baltimore: The Williams & Wilkins Company, 1959, $20.00.

This book represents the first attempt to collect information on the specialized subject of pediatric pathology within a single volume. Since the author uses the clinical approach in many of his discussions, the book should be of interest to the pediatrician as well as the pathologist.

Many topics are covered, some too briefly. The text begins with a presentation of disorders peculiar to the period of growth and development, moves on to include a discussion of congenital malformations and the rapidly expanding field of inborn errors of metabolism, and then proceeds in standard fashion to a description of the various categories of disease. The mystery of sudden death in infants in whom there are no significant autopsy findings remains unsolved, although the author offers a theory of his own.

The illustrations, taken primarily from the extensive files of the Armed Forces Institute of Pathology, are of excellent quality. It, however, would have added to the book if more of the photographs could have been of gross specimens. The reviewer was surprised to find many misspelled words throughout the text. The Appendix is of interest in that it gives an analysis of the first 10,000 cases entered in the files of the American Registry of Pediatric Pathology for the period 1954–1956. As the author points out, this list does not necessarily indicate the frequency of these diseases in the general population.

GRACE H. GUIN, M.D.

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